

Attachment D1 – 21 CFR Part 7, Guidance to Health Hazard Evaluation Committees

The Food and Drug Administration's recall policy (21 CFR Part 7) requires the conduct of an evaluation of the health hazard (actual or potential) presented by a product being recalled or considered for recall. The regulations (21 CFR 7.41(a)) specify the factors to be considered, among others, by the Health Hazard Evaluation Committee in making the health hazard evaluation. The purpose of the health hazard evaluation, in general, is to identify and document:

1. the population at risk,
2. conditions that may exacerbate or attenuate the risk of its occurrence,
3. the risk associated with the product under conditions of use (as labeled),
4. and the likelihood of the risk occurring in the future.

The purpose of these guidelines is to assist the Committee in the identification and documentation of the various factors listed in 21 CFR 7.41(a) that are to be considered in making the health hazard evaluation and to determine what additional data and information should be collected and evaluated during the recall either to confirm or revise the health hazard evaluation. The questions listed below are not all inclusive nor are they relevant to all recall situations. They are intended to focus attention on factors related to the significance of health hazards likely to be associated with a product being recalled or considered for recall.

7.41(a)(1) - Whether any disease or injuries have already occurred from the use of the product.

1. What is the name of the product (trade and generic) and what are its indications for use, where applicable?
2. What deaths, diseases, injuries, or other adverse reactions have already occurred in association with use of the product?
3. What documentation is there to support the association of the deaths, diseases, injuries, or other adverse reactions with the use of the product?
4. Was the product used in conformance with its labeled directions for use? (The Health Hazard Evaluation Committee should review product labeling for sufficiency in light of injuries). If not, did the deaths, diseases, injuries, or other specific adverse reactions result from product misuse?
5. If the product was used according to its labeled directions, were the associated diseases, injuries, deaths, or other specific adverse reactions due to a) product malfunction, b) product formulation, c) product quality (including potency, contamination, etc.), d) product design, e) inadequate directions for use, or f) other known or unknown causes? Specify.

7.41(a)(2) - Whether any existing conditions could contribute to a clinical situation that could expose humans or animals to a health hazard.

Any conclusion shall be supported as completely as possible by scientific documentation and/or statements that the conclusion is the opinion of the individual(s) making the health hazard determination.

1. Name the specific clinical conditions (e.g., diabetes, heart problems, etc.) which, if they exist, might render a person or animal more susceptible to experiencing a health hazard on exposure to the product.

2. How would these clinical conditions contribute to or change the risk of exposure to the products?
3. Could these clinical conditions mask or otherwise disguise the risk of exposure to the product?
4. What other products being used to treat these clinical conditions could contribute to or, conversely, lessen the risk of exposure to the product?

7.41(a)(3) - Assessment of hazard to various segments of the population, e.g., children, surgical patients, pets, livestock, etc., who are expected to be exposed to the product being considered, with particular attention paid to the hazard to those individuals who may be at greatest risk.

1. What is the universe of users by segment of population and what is the relative frequency of use of each, if known. For example, what percentage of the product is used by infants or children?
2. Which segment of the population exposed to the products is at greatest risk of health hazard? Others above risk for "normals?"
3. Are any of the following high-risk groups likely to be exposed to the product?
 - a. Infants
 - b. Children
 - c. Elderly
 - d. Pregnant Women
 - e. Surgical patients
 - f. Others (specify)
4. For each of the high-risk groups identified, what is the anticipated frequency of exposure to the product?
5. In what setting is the product generally used (e.g., hospital, home, etc.)?
6. How frequently is the product used (e.g., daily, weekly, etc.) and what is the duration of use (e.g., one time only, for a month, over a lifetime, etc.)?
7. What percentage of the population at greatest risk is now under close medical supervision? Could everyone in this population be easily brought under observation? In practice, would all users be brought under medical supervision if this is needed?
8. What actions or medical interventions could reasonably be expected to decrease the likelihood of occurrence of the health hazard? For example, could patient monitoring detect the product defect before it causes any untoward health consequences and could patient monitoring entirely prevent medical injury?

7.41(a)(4) Assessment of the degree of seriousness of the health hazard to which the population at risk would be exposed.

1. Are the health hazards likely to be acute (lasting several days to a few weeks) or chronic (lasting weeks to months)?
2. Describe the degree of seriousness of the health hazard if it did occur, and which specific segment of the population might be at risk? Express in terms of the following:
 - a. Life threatening - death could occur
 - b. Severe - permanent significant disability
 - c. Moderate - transient but significant disability; permanent minor disability
 - d. Limited - transient minor disability; annoying complaints
 - e. None - no disability or physical complaints anticipated

7.41(a)(5) - Assessment of the likelihood of occurrence of the hazard.

1. How frequently have deaths, diseases, injuries, or other adverse reactions already occurred? How does the frequency of occurrence relate to the total extent of product exposure (e.g., number of devices implanted, number of prescriptions, etc.). How has this frequency been documented?
2. If deaths, diseases, injuries, or other adverse reactions have not already occurred, estimate the likelihood of occurrence in each segment of the population at risk.

7.41(a)(6) - Assessment of the consequences (immediate or long range) of occurrence of the hazard.

1. What are the immediate consequences of the health hazard?
2. What are the long-range consequences of the health hazard?
3. If the product being recalled or considered for recall is used to treat a medical condition, are alternate forms of therapy available?

SUMMARY OF HEALTH HAZARD EVALUATION

On the basis of the answers to the questions listed above and any others that relate to the associated risk, state the likelihood of the health hazard occurring following exposure to the product being recalled or considered for recall and the likelihood of exposure to a defective product in all users of the product.

In addition, include in the recommendation specific data and information that should be collected, how and by whom these should be collected and evaluated, and how frequently the health hazard should be reevaluated.